REMARKS

An appropriate request for an extension of time is submitted herewith. A Request for Continuing Examination is also submitted herewith. If the extension and/or RCE is missing, please consider this paper to be a request for such extension and deduct any required fee from deposit account 10-1205/FINE:002CON1.

Claim amendments

Claim 43 has been rewritten in independent form, introducing no new issues of patentability.

New claim 51 is based on a combination of claim 1 as filed and the additional feature that the zones are not separated by a barrier material. This is implicitly disclosed as a possibility within the invention by claim 45 which is directed to the opposite scenario where such a barrier material is present. The absence of such a barrier material is also a feature of the examples. The current objections under 35 USC § 103(a) are all based in part on Bakulesh et al, which does not disclose any manner of formulation in accordance with claim 51.

Claim rejections - 35 USC § 103

1) Claims 1-11, 19-26, 32-48 and 50 stand rejected under 35 USC § 103(a) as unpatentable over Glagau et al (DE 10206995 in machine translation) in view of Runge et al (WO 99/57242 – using US 7,307,708 as translation) and Bakulesh et al (GB2323532).

The Examiner remarks that Glagau et al teach a two-part micronutrient product, useful as a dietary supplement and for treatment of disease. The Examiner goes on to state that Glagau teaches that 'The product may be formulated as multi-component single tablet (sic).' We respectfully dispute that quoted statement. Glagau et al nowhere contains such a statement in terms. The Examiner refers to page 5, 4th paragraph. That reads as follows:

'Preferably the Probiotika contained micro-nutrient combination product of comprising at least two products with different composition is present in the form of 0-10 tablets, preferably 1 to 5 tablets, 0 to 10 capsules, preferably 1 to 5 capsules, 0 to 5 solutions, preferably 1 to two solutions and/or 0 to 5 granulates, preferably 1 to 3 granulates'.

Thus, the cited passage does not contain the statement made by the Examiner. Instead, the cited passage calls for two discrete components, such as one tablet and one capsule, one capsule and one solution, and so on. In this regard see the attached Rule 132 Declaration of Marianne Winning (hereinafter, the "Rule 132 Declaration"), especially paragraph 21. The Rule 132 Declaration is incorporated in its entirety into this paper by reference.

The Examiner notes at page 5, line 3 of the Office Action that Glagau et al does not explicitly disclose a zoned single tablet, but argues that part of a motivation based on the combined art to make a zoned single tablet would stem from Glagau et al because Glagau et al 'includes a formulation of the multi-component product that includes the form of one tablet, as well as the need to keep the probiotic separate from the nutrients in the second component.
We submit that Glagau et al does not just fail explicitly to disclose a zoned single tablet but that Glagau et al does not suggest such a tablet indirectly or implicitly and that Glagau et al actually teaches away from such a concept. We submit that the no motivation would be derived by one of ordinary skill in the art to make a single zoned tablet based on the teachings of Glagau et al (see the Rule 132 Declaration, especially at paragraph 11-13, and 21).

We submit that the cited passage of Glagau et al would be understood as meaning only that (in the particular instance when there are two components) the two components need to be physically separate and distinct components and that one may freely choose between two tablets or one tablet with one other kind of formulation such as granulate, solution or capsule.

Nowhere does Glagau et al suggest that one unit of one kind of formulation can provide all of the needed components. Glagau et al teaches that the components must be kept separate and does not anywhere suggest that a sufficient degree of separation can be achieved within one unit of one kind of formulation, such as in a single zoned tablet.

Moreover, a single tablet is not consistent with the teaching of Glagau et al taken as a whole. Thus, the passage in issue relates to the provision of at least two products, which Glagau et al

teaches are to be kept separate. But earlier, at page 5, paragraph 2, it is indicated that having separate products presents the advantage that the products can be administered separately. This of course becomes impossible if one formulates both separate products into one tablet as separate zones.

Thus, when Glagau et al teaches that the two components are separate, it is meant that they are separate such that they can be administered separately, not that they form zones within one product unit.

The point of the separate administration is explained in this passage as being that it allows the probiotic composition to be taken first so as to populate the small intestine. They are to be administered separately from meals and the other composition so that production of gastric acid does not kill off the probiotics. Then, the administration of the trace elements in the other composition results in improved absorption of these trace elements because of the now established activity of the lactic acid producing bacteria in the intestine.

This suitability for separate administration is expressed in Glagau et al in this passage to be a universal property of the compositions that it teaches, thus excluding one tablet from being within the scope of the invention as envisaged and as taught by Glagau et al.
Thus, taken as a whole, Glagau et al does not 'include' within its teaching even in an unspoken manner the concept of one zoned tablet.

Even if per arguendo it was taken that Glagau et al did in this unspoken sense include the possibility of one zoned tablet, Glagau et al would not motivate a reader of ordinary skill in the art to produce such a product or contribute to any motivation in that direction in any combination of art.

The provision of a single product unit is also contrary to the direction of teaching in Glagau et al at page 4, final paragraph, which teaches that preferably there should not just be two separate products present but at least three or at least four separate in form.
The Examiner argues that Bakulesh et al teaches a multi-zoned tablet containing a probiotic kept separate from secondary active ingredients by barrier materials. We submit that this summary of the teaching of Bakulesh et al is over broad and that the teaching is in fact limited to tablets containing a probiotic kept separate from an anti-infective and does not include any

teaching of keeping a probiotic separate from 'a nutritionally active ingredient' in general nor any of the particular nutritionally active ingredients stipulated in claim 1 as amended in this response.

Equally, the anti-infective agents of Bakulesh et al are not the same as the secondary ingredients of Glagau et al. (see the Rule 132 Declaration, especially at paragraph 17). Glagau et al is concerned with separating probiotics from (see Example 1) vitamins, selenium and metals including iron, zinc, manganese, copper, chromium, and molybdenum, iodine, carotenoids, bioflavonoids, and inulin. Adequate protection from anti-infectives if provided in Bakulesh et al could not be equated to providing adequate protection from the most active and deleterious of these different ingredients. The anti-infectives of Bakulesh et al are relatively large molecules, whereas some of the ingredients against which protection is needed in Glagau et al and in the present invention are metals which would be present as ions. As the Applicant's specification describes, encapsulation is not sufficient to protect probiotic micro-organisms from inter alia those given in 'List A' on page 4, i.e. encapsulated iron and encapsulated copper.

Furthermore, it should be recognised that the reader of ordinary skill in the art will note that Bakulesh et al is a proposal completely lacking in any evidence for its effectiveness (see the Rule 132 Declaration, especially at paragraph 19. All the examples are written in the present tense, generally accepted as indicating that they are not reporting work actually done but are prophetic This is supported by the fact that no results by way of actual measurements are provided regarding the stability of the described formulations, merely assertions. Moreover, at least some of these assertions can be seen immediately to be far-fetched. The assertion that a reconstituted solution of anti-infective containing probiotic micro-organisms would remain viable for 3-7 days seen at page 22, penultimate paragraph clearly casts doubt on all of the results forecast.

We submit that it would not have been obvious based on a combination of Glagau et al and Bakulesh et al to make a single tablet containing in two zones the probiotic and the secondary ingredients of Glagau et al and that if such a product were to be conceived of, the person of ordinary skill in the art would not have had a reasonable expectation that such a product would provide satisfactory protection of the viability of the probiotic.

The Examiner has argued at page 11, third paragraph, that because Glagau et al provides for a product that can be a single tablet and Bakulesh et al teaches a multi-zoned tablet, then the provision of a multi-zoned tablet in which probiotics and nutritive components are kept separate is a known option and that this therefore makes it a known viable option. However, it clearly cannot follow that this is a known viable option when neither teaching purports to have tested it for viability. Any expectation as to whether the untested option is viable would have to depend on a technical assessment of the problem and the weight of evidence for viability to be found in the combined documents. It cannot follow from the alleged known status of the option that the option is a viable one. For the reasons given above, the option would not have been expected to be viable. Indeed, absent special practice regarding water content and activity, the option of putting the Glagau et al ingredients into one multi-zone tablet would indeed not have been viable.

Neither Glagau et al nor Bakulesh et al contains any teaching regarding water content and activity. For this aspect of the invention, the Examiner relies on Runge et al. Runge et al however is not a teaching relating to the situation envisaged by the Examiner of a single tablet containing both probiotic and at least one nutritionally active ingredient, or more particularly one as required by claim 1 as now amended. US 6,254,886 (Fusca et al) however, discussed in the Applicant's specification, does teach directly how to control water content to achieve sustained viability in such formulations.

Accordingly, when it comes to water content and water activity, the skilled reader has the choice of two teachings, one of which is directed to the problems associated with maintaining the stability of compositions containing problem ingredients and one of which is not. Given this choice, the skilled reader clearly would follow the teaching of Fusca et al in preference to that of Runge et al.

The Examiner argues that it would have been obvious to follow Runge et al because Runge et al teaches that the given parameters for water content and activity are beneficial for viability and shelf life. Runge et al does not however teach or suggest that this would be true outside of the context of a preparation that does not contain any of the problem ingredients with which the invention is concerned. The Examiner states that the person of ordinary skill in the art would look to teachings in the art of dried probiotics (page 13, first paragraph). We contend that the

skilled person would look to the most relevant of those teachings, i.e. to those dealing with the stability of formulations of probiotics with other nutritionally active ingredients, i.e. to Fusca et al.

The Examiner quotes KSR /Great Atlantic for the proposition that if a technique has been used to improve one device (here the formulation of probiotic alone) and a person of ordinary skill in the art would recognise that it would improve similar devices in the same way, using the technique is obvious... . However, in this case, a skilled worker would not recognise that the water content and activity conditions of Runge et al would improve the allegedly 'similar device' constituted by a tablet containing both probiotic micro-organisms and other nutritionally active ingredients. On the contrary, given the skilled worker's knowledge of the special problems of maintaining the viability of micro-organisms in such products and knowledge that these problems extend beyond those encountered in formulations of micro-organisms in the absence of such additional nutritionally active ingredients (as witnessed to by Fusca et al), the skilled worker would have had no expectation that the conditions of Runge et al for a starter culture would be beneficially applied to a multi-zone tablet containing the ingredients of Glagau et al.

Contrary to the Examiner's assertion, it would not have been obvious that the water conditions taught to be beneficial for one kind of tableted probiotic composition (Runge et al) would have been good also for a different type of probiotic composition (constructed from a combination of Glagau et al and Bakulesh et al) – see the Rule 132 Declaration, especially at paragraphs 13-14.

The Examiner has stated at page 14, second paragraph that this line of argument is not persuasive because the teaching of Runge et al is applicable to any formulation that contains a probiotic and wishes to maintain its viability. That statement is not justified by the Examiner by any reference to any passage of Runge et al. We submit that Runge et al contains no such teaching that it is applicable to extend the viability of any formulation containing a probiotic.

Runge et al is directed to making starter cultures for preparing foodstuffs and feedstuffs, which is a different field from making tablets and other forms for oral consumption as in Glagau et al and Bakulesh et al. Such starter cultures do not contain the problem ingredients iron, copper, vitamin B6, zinc, manganese, chromium, pantothenic acid and pantothenic acid salts. Nothing in Runge et al suggests that the described composition could be modified to include such further ingredients and remain stable on storage as regards micro-organism viability. Nowhere

is it stated in Runge et al that the described water parameters are applicable to any end-formulation that contains a probiotic for which viability is to be maintained.

Against our previous submissions regarding the expectation of success in applying the water parameters of Runge et al to a multi-zone tablet, the Examiner has objected that these were merely Attorney argument unsupported by evidence or declarations of those skilled in the art. We accordingly submit herewith the Rule 132 Declaration by one of the inventors, Marianne Winning. This Rule 132 Declaration supports the arguments previously made by Counsel as well as the comments made in this paper.

The Examiner has further commented that there is nothing in the cited prior art references that suggests that keeping the probiotic formulations at a water content and activity favourable for probiotic viability would have caused the additional ingredients if kept separate in a multi-zone tablet to become endowed with properties that would render the composition unstable as is said to be asserted by the Applicant. However, we submit that this is exactly what the prior art references taken as a whole (so as not to exclude the relevant teaching) do indicate. Thus, we have drawn attention to Fusca et al. (see the Rule 132 Declaration, especially paragraph 18. Fusca et al.specifically teaches that maintenance of a water content of not more than 0.1% is a necessity when multilayer tablets are formulated containing effective amounts of nutritional ingredients to provide inter alia trace elements (column 2, line 33).

The consideration of whether the prior art contains teaching incompatible with the suggested combination should not be limited to the cited prior art so as to exclude those incompatible teachings which would also be within the knowledge of the worker of ordinary skill in the art and which would shape the opinion of the skilled worker as to what would be likely to work and what would not.

The Examiner has further argued that dried probiotics perform best under optimal moisture conditions and that the presence of deleterious ingredients does not change the fact that the probiotics will perform best when the moisture content is optimal. However, it was not the expectation prior to the invention of the worker of ordinary skill in the art that there was one set of conditions that universally would be optimal for probiotic micro-organisms whether in the presence of deleterious ingredients or not, see the Rule 132 Declaration, especially at paragraph 20. On the contrary, there were different teachings relating to the moisture

parameters which were considered best for these two different situations (Fusca et al vs Runge et al). Since the conditions which would be optimal for two zone compositions containing deleterious ingredients were identified in Fusca et al, it is those conditions which would have been used and nothing in the art suggested that the extreme drying used in Fusca et al could be avoided in such compositions without unacceptable loss of viability on storage. The combining of teachings made by the Examiner is not done on the basis that together they indicated that the water parameters claimed are optimal for probiotic micro-organisms in multi-zone tablets containing deleterious ingredients. The references together or separately have nothing to say about what conditions would be optimal for such a formulation. Rather, the references have been selected entirely on the basis of hindsight with a view to finding conditions as claimed (in Runge et al) and transferring those conditions to formulations as claimed (assembled by combining Glagau et al and Bakulesh et al).

Claim 43 has been included within this rejection even though it requires a water activity of no more than 0.02 and Runge et al fails to disclose a water activity below 0.03. No reason for selecting a water activity lower than 0.02 in combination with a water content of at least 0.2% has been put forward by the Examiner. We accordingly submit that the rejection of claim 43 has not been justified.

2) Claim 2 stands rejected under 35 USC § 103(a) as being unpatentable over Glagau et al in view of Runge et al and Bakulesh et al and further in view of Belicova et al.

Belicova et al is cited to show use of selenium. Claim 2 is inventive by virtue of its dependency on Claim 1 and Belicova et al does nothing to remove the deficiencies of the primary references discussed above. Furthermore, Belicova et al contains no teaching relevant to any effect that selenium might or might not have on the stability in terms of storage viability of a dry formulation of micro-organisms. No dry micro-organism formulations are described and even the cell-suspensions described on page 302, mid page, are stored at 4 oC and are used within one day. The study is concerned with the anti-mutagenic effect of selenium in culture in the presence of mutagens, not with dry formulations and viability in the absence of mutagens.

3) Claim 32 stands rejected under 35 USC § 103(a) as being unpatentable over Glagau et al in view of Runge et al and Bakulesh et al and further in view of Andoh et al.

Andoh et al is relied upon to show a multi-granule tablet. Claim 32 is inventive by virtue of its dependency on Claim 1 and Andoh et al does nothing to remove the deficiencies of the primary references discussed above.

4) Claim 50 stands rejected under 35 USC § 103(a) as being unpatentable over Glagau et al in view of Runge et al and Bakulesh et al and further in view of Cavaliere et al.

The objection is in our submission inadequately supported. First, Cavaliere et al is relied upon to show a multi-layer tablet where the layers have different release rates. Claim 50 is inventive by virtue of its dependency on Claim 1 and Cavaliere et al does nothing to remove the deficiencies of the primary references discussed above.

Secondly, Cavaliere et al discloses tablets in which both layers contain the same micro-organisms and neither layer contains the deleterious ingredients specified in claim 1. Nothing in the cited art teaches that any advantage is to be gained by having faster and slower releases of probiotic micro-organisms on the one hand and deleterious ingredients on the other hand. Moreover, no cited art discloses the desirability of the micro-organism containing zone being the one which releases faster than the other.

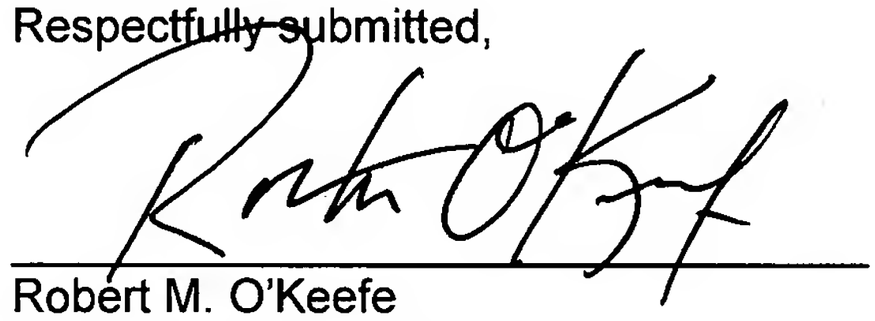
We respectfully request allowance of the present claims.

CONCLUSION

In view of the foregoing, it is submitted that the claims are in condition for allowance. Accordingly, favorable reconsideration and Notice of Allowance are courteously solicited.

Should any fees under 37 CRF 1.16-1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct such fees from Deposit Account No. 10-1205/FINE:002CON1. The examiner is invited to contact the undersigned at the phone number indicated below with any questions or comments, or to otherwise facilitate expeditious and compact prosecution of the application.

Respectfully submitted,



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